

WHASC – Animal Final Report

1May2012

1. Protocol Number: FWH20090166A**2. Type of Research:**

1) Animal Research

3. Title:

“A Comparison of Proximal Tibia, Proximal Humerus and Distal Femur Infusion Rates of Blood Under High Pressure Using the EZ IO Intraosseous Device on the Adult Swine (Sus scrofa) hypovolemic Model.”

4. Principal Investigator (PI):

| Name | Rank | Date of IACUC Training | Branch of Service/ Corps | Staff Resident Fellow Civilian | Department / Office Symbol | Email (if other than WHASC Outlook) | Phone | Pager |
|--------------|-------|------------------------|--------------------------|--------------------------------|----------------------------|-------------------------------------|-------------------------------|--------------------|
| Julio Lairer | LtCol | 26 Oct 2009 | MC | Staff | 59th EMDS/SG O3D | | WP: 916-7836 FAX: 292-7649 | Cell: 210-867-0848 |

5. Purpose:

The purpose of this study is to evaluate the use of blood product administration through an IO under pressures >300mmHg. A secondary objective of this study will be the establishment of which IO site between the proximal tibia, proximal humerus and the distal femur can reach the higher flow rates. Data from Lairer et al. have postulated that the proximal humerus appears to deliver higher flow rates than the other two sites. This fact also needs to be validated.

6. Results:

The mean maximum infusion pressure was 538 mmHg (SD 80 mmHg) for the humerus, 630 mmHg (SD 80 mmHg) for the femur, and 650 mmHg (SD 76 mmHg) for the tibia. The mean infusion rate for the tibia was 78 mL/min (SD 38.5 mL/min), 49 mL/min (SD 45.1 mL/min) for the femur and 103 mL/min (SD 34.1 mL/min) for the humerus. Infusion rate comparison of all the sites using ANOVA revealed a $p < 0.005$. Comparing the infusion rates of the humerus (103 mL/min) to the femur (49 mL/min) revealed a $p < 0.01$. Comparisons between the tibia with the humerus and femur did not reveal statistical significance. All the animals in the tibia arm survived to the end of the experiment; in the femur and humerus arms the survival rate was 12/14 (86%) and 11/14 (79%) respectively. In the tibia and humerus arms the serum lactate increased during the hypovolemic period and decreased after infusion of blood. In the femur arm the serum lactate increased until the experiment ended. Histopathologic examination revealed that fat emboli were present in 14/14 (100%) of the tibia arm, 10/11 (91%) of the humerus arm (samples from 3 swine were inadequate), and 8/14 (57%) of the femur group.

For the proof of concept portion of the protocol amendment #2

The baseline MAP were similar (Table). After removal of the blood the mean MAP at hypotension were also similar (Table) Comparison of the MAP for the post hydroxocobalamin administration groups using ANOVA revealed a $p < 0.001$. Post HOC analysis using the Tukey honestly significant difference (HSD) between groups revealed statistical difference between group 1 to groups 2 and 3 ($p < 0.001$) but not when comparing groups 2 and 3 ($p < 0.844$). The baseline SVR prior to removing the blood for group 1 was 841.5 (SD 36), group 2 - 975 (SD 24) and group 3 - 642.5 (SD 3.5). At hypotension the mean SVR was similar in all 3 groups. The mean SVR for each group in the 90 min post administration of hydroxocobalamin was 1025 (SD 194) for group 1, 1099 (SD 135) for group 2 and 726 (SD 130) for group 3. Comparison of the post hydroxocobalamin administration groups using ANOVA revealed a $p < 0.001$. The baseline Heart Rate (HR) prior to removing the blood for group 1 was 96.5 (SD 19), 75 (SD 10) for group

For Protocol Office Use Only:

Received on: _____ Initials _____ Report Due Date _____ Scheduled for IACUC: _____

Copy to Budget? Yes No BIRDS Agenda Who Signed? PI Co-PI Auth AI

For Review Purposes Only

Eligible for Expedited Approval? Yes No Signature _____ Date: _____

2 and 76 (SD 10) for group 3. After removal of the blood the mean HR for group 1 was 96 (SD 25), 95.5 (SD 5) for group 2 and 78.5 (SD 0.7) for group 3. The mean HR for each group in the 90 min post administration of hydroxocobalamin was 106 (SD 7) for group 1, 90 (SD 5) for group 2 and 83 (SD 13) for group 3. Comparison of the post hydroxocobalamin administration groups using ANOVA revealed a $p < 0.001$.

| | Mean Baseline MAP | Mean MAP after at 50% MAP | Mean MAP after hydroxocobalamin administration | % return back to baseline at 90 minutes |
|---------|-------------------|---------------------------|--|---|
| Group 1 | 83 (SD 1.4) | 41 (SD 3.1) | 87 (SD 23) | 105 % |
| Group 2 | 67.5 (SD 3.5) | 34.5 (SD 2.1) | 61 (SD 3.5) | 90 % |
| Group 3 | 77 (SD 15.6) | 38 (SD 5.7) | 60 (SD 4.5) | 78 % |

Conclusion: Intraosseous hydroxocobalamin significantly increased mean arterial blood pressure and systemic vascular resistance in our pilot, dose-finding hemorrhagic shock swine model. The blood pressure response paralleled increasing drug dose. Hydroxocobalamin may prove to be a pharmacologic adjunct for hemorrhagic shock.

7. How may your findings benefit the Air Force?

The results of this study suggest that the humerus may be a better site for administration through an intraosseous device. The fact that fat emboli were seen in the lungs needs to be further studied as this finding if confirmed would suggest that intraosseous devices might only be used in emergency situations.

The information learned from the proof of concept has allowed Lt Col Beberta to apply and receive a research grant to further study the concept of administering hydroxocobalamin for hemorrhagic shock.

8. Number of Animals

Projected Enrollment of Animals at the Beginning of Study: **46**

Amendment 2: **Added 6 animals** as a proof of concept model to use hydroxocobalamin for hemorrhagic shock.

Amendment 3: Requested an **additional 3 animals** for repeat of the first 3 animals of the femur arm. It was discovered that the length of the IO needle was not adequate to get the needle into the proper location of the bone for re-infusion of the blood.

Actual Number of Animals Enrolled: **55**

9. Status of Animals Entered Into the Protocol:

All animals were in good general health and were euthanized per protocol.

10. Status of Funds:

All funds were executed.

11. Reason for Closure:

Objectives of the study were met

12. Specific Problems:

During the femur arm we discovered that the needle length was not long enough to reach the marrow of the bone. This was corrected by performing dissection to the bone prior to placement. No issues were encountered after this correction of technique.

13. Publications and Presentations:

None

Presentations:

None

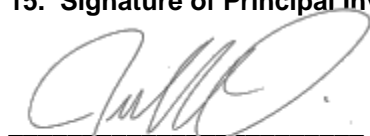
Publications:

None

14. Exceptional Achievements:

None

15. Signature of Principal Investigator:



Julio Lairet, Maj, USAF, MC
Director Enroute Care Research Center

For Protocol Office Use Only:

Received on: _____ Initials _____ Report Due Date _____ Scheduled for IACUC: _____

Copy to Budget? Yes No BIRDS Agenda Who Signed? PI Co-PI Auth AI

For Review Purposes Only

Eligible for Expedited Approval? Yes No Signature _____ Date: _____

